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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/930,335 | 08/15/2001 | Graham Paul Matthews | 4-30811A/C1 | 1679 |

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| KWON, BRIAN YONG S | |
| ART UNIT | PAPER NUMBER |
| 1614 | |

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/930,335 | MATTHEWS ET AL. | |
| | Examiner | Art Unit | |
| | Brian S. Kwon | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *9-13* is/are pending in the application.

4a) Of the above claim(s) *10,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application*

1. Applicant's arguments filed August 07, 2006 have been fully considered but they are not persuasive.

2. Claims 9-13 are currently pending in the application, but claims 10, 12 and 13 has been withdrawn from further consideration by the examination as being drawn to a non-elected invention.

3. Looking at the prosecution history, the examiner required restriction requirement between product and process claims (see O.A. mailed June 18, 2002), and subsequently applicant elected product claims as the elected invention.

Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102,

103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claim 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (EP 0733372 A2 or its English equivalent to US 5726164).

Weder teaches a composition comprising N-benzoyl-staurosporin, a hydrophilic component (e.g., ethanol and water), surfactant such as polyoxyethylene/polyoxypropylene block copolymer (e.g., Pluronic F68 and Lutrol F68), lipophilic component such as phospholipids, in particular purified lecithin from soybeans (e.g., LIPOID S 100), and additives (e.g., glycerol and sorbitol), wherein said composition produces a suspension of colloidal nanoparticles (abstract; column 2, line 60 thru column 6, line 8; column 7, lines 40-42; Examples 1-3).

The teaching of Weder differs from the claimed invention in (i) the specific amounts active and inactive ingredients (claim 9) and (ii) "bioavailability levels of N-benzoylstaurosporine of from 5 to 17%", "AUC...of from 380 to 2000", and "Cmax...of from 60 to 310" (claim 11). However, those of ordinary skill in the art would have readily optimized

effective dosages as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose or dosage having the desired bioavailability, AUC, and Cmax of the active ingredient may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage or the appropriate pharmacokinetic of N-enzoylstaurosporine for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed herein

***Response to Arguments***

5. Applicant's arguments filed August 07, 2006 have been fully considered but they are not persuasive.

Similar to the argument filed December 13, 2005, the applicant's argument in the response filed August 07, 2006 takes the position that one skilled in the art would not accept the teachings of Weder. The Applicant alleges that there is no suggestion that one could gain from the teaching of an injectable form, such as that of Weder et al., that would lead one to design an oral form, such as that of the Applicant's invention.

This argument is found unpersuasive. Although the Weder generally discloses the preparation of the staurosporin derivative (i.e., N-benzoyl-staurosporin) in intravenous injectable formulation, the Weder acknowledges that there exist general art accepted knowledge in preparing the staurosporin derivative in oral dosage forms (see column line 44 thru column 2,

line 9). In fact, the oral dosage forms containing said staurosporin derivative were well known at the time of the invention was made (see EP 657164 A1 or US 5736542). Furthermore, all the secondary ingredients employed (i.e., hydrophilic component, lipophilic component and surfacts) herein are known to be useful as formulation base that is suitable for intravenous dosage forms and oral dosage forms. Thus, one having ordinary skill in the art at the time of the invention was made would have known that said staurosporon derivative (i.e., N-benzoyl-staurosporin) would be formulated into various dosage forms including oral or intravenous depending upon the convenience of the patients and clinical practitioners.

The applicant's argument in the response takes the position that the claimed invention provided superior unexpected activity. Applicant alleges that the highest plasma concentration (0.36 and 0.45 μMol/l at 3$^{rd}$ hour (tmax) for an oral dosage of 100mg of N-benzoylstaurosporine which is disclosed in Henry is less than the instantly claimed formulation that provides Cmax of plasma concentration of 0.486-1.212 μMol/l with most tmax about 2$^{nd}$ hour for a only 50mg dosage (Table 2).

This argument is not persuasive. The applicant's alleged superior unexpected activity cannot be considered proffered evidence to overcome the rejection of the record since the unexpected results is not based on comparison with the Weder's formulation which is the instant rejection is relied upon. Thus, the applicant maintains that the Weder makes obvious the instant invention.

*Conclusion*

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

AU 1614

BRIAN-YONG S. KWON
PRIMARY EXAMINER